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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,567	07/11/2003	Leong Ng	ISA-004.01	3759

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/618,567	NG, LEONG	
	Examiner	Art Unit	
	James L. Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-21 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-21 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4/19/04;9/09/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The prior art, such as the references of Totsune et al. or Wilkinson et al., suggest that elevated levels of urotensin II are found in samples obtained from a variety of patients and that detection of such elevated levels in such a patient would not indicate a risk of heart failure in that patient. Thus, absent further written description and guidance from applicant, one would not be assured of the ability to assess a risk of heart failure in patients based merely upon detection of elevated levels of urotensin II in a sample from a patient not known or suspected of having heart failure or a risk therefor.

Moreover, it is not clear from the instant disclosure or the prior art, e.g. Douglas et al. (2002), if elevated levels of urotensin II are indicative of a risk for, or are merely a result of,

heart failure because the elevated levels appear to have been detected only in patients after the occurrence of heart failure. Further unpredictable experimentation would appear to be required to determine a predictive relationship of urotensin II levels with RISK of heart failure. Thus, absent further written description and guidance from applicant, one would have no assurance of the ability of urotensin II levels to predict heart failure prior to the occurrence of the failure, i.e. to detect a risk for, rather than the presence of, the condition.

Claims 1, 2, 6-9, and 13-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Applicant teaches competitive immunoassay of extracted plasma samples for determination of urotensin II. Applicant provides no written description or guidance for other than immunoassay determination of the marker and one would not readily know what other method predictably functions for the determination of this or the second marker. Further unguided unpredictable experimentation would appear to be required to identify an alternative to immunoassay. Absent further description and guidance from applicant, one would not be assured of the ability to predictably practice the determination with other than the disclosed immunoassay.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 and claims dependent thereupon, "the" level or normal level lack antecedent basis. The interrelationships of the components and steps of the method are not clear, e.g. there is nothing to connect the subject to either the sample or the indication of risk. A method claim should clearly state each component used in the method and the relationship of the various components. A method claim should also conclude with a step relating the method result to the purpose of the method, preferably to the purpose as also set forth in the preamble of the claim.

In claim 2, "the result" lacks antecedent basis.

Claim 3 provides for using an immunoassay, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 10 provides for the use of an immunoassay, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 11 and 12 duplicate the subject matter of claims 4 and 5, respectively. In these claims, "the" immunoassay lacks antecedent basis in claim 1. In claims 4 and 5, it is believed

that claim --3-- was intended. In claims 11 and 12, it is believed that claim --10-- was intended. Moreover, in claims 5 and 12, it is believed that --method-- was intended.

In claim 6, "typically" is not defined and it is not clear what level is encompassed within the metes and bounds of the invention. Moreover, in this claim "the absence" lacks antecedent basis.

In claim 18 and claims dependent thereupon, "the" detecting lacks antecedent basis.

In claim 19, "the" level lacks antecedent basis.

In claims 20 and 21, "the" second marker lacks antecedent basis in claim 18, it is believed that claim --19-- was intended.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(f) he did not himself invent the subject matter sought to be patented.

Claims 1-6, 11, 12, and 18 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Totsune et al. (Lancet 358: 810, 2001).

Totsune et al. detected levels of urotensin II in patient and normal plasma samples with an immunoassay using anti-human urotensin II antibodies.

Claims 1-6, 11, 12, and 18 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Wilkinson et al. (Cardiovasc. Res. 53: 341, Feb. 2002).

Wilkinson et al. detected levels of urotensin II in plasma samples with an immunoassay using anti-urotensin II antibodies.

Claims 1-21 are rejected under 35 U.S.C. § 102(f) because the applicant did not invent the claimed subject matter. Ng et al. (Circulation 106: 2877, 2002) teach the invention essentially as claimed and provide evidence of an inventive entity other than the inventive entity as instantly set forth.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-6, 11, 12, and 18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Culp et al. (US 6,075,137) in view of Douglas et al. (Lancet 359: 1990, June 2002), and either or both of Totsune et al. or Wilkinson et al.

Culp et al. teach detection of urotensin II in patient samples by immunoassay for diagnosis of, or diagnosis of susceptibility to, a disease, particularly heart failure (see e.g. col. 8). The reagents for the assay can be provided in a diagnostic kit. However, the reference did not specifically exemplify detection of urotensin II in a body fluid sample.

Douglas et al. teach elevated levels of urotensin II in patients with heart failure.

The teachings of Totsune et al. or Wilkinson et al. are as set forth above, teaching immunoassay detection of urotensin II in plasma samples.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have used the immunoassays of Totsune et al. or Wilkinson et al. in the method of Culp et al. for the diagnosis of, or diagnosis of susceptibility to, heart failure in a patient in view of the direct suggestion in the reference to do so. One of ordinary skill in the art would have had a reasonable expectation of success in view of the teachings of Totsune et al. or Wilkinson et al. that urotensin II can be detected in plasma and because Douglas et al. taught that urotensin II was elevated in patients with heart failure.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Claims 1-21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Culp et al. (US 6,075,137) in view of Douglas et al. (Lancet 359: 1990, June 2002), and either or both of Totsune et al. or Wilkinson et al. as applied to claims 1-6, 11, 12, and 18 above, and further in view of Hall (Eur. J. Heart Failure 3: 395, 2001) and either or both of Karl et al. (Scand. J. Clin. Lab. Invest. 59 (Suppl. 230): 177, 1999) or Hunt et al. (Clin. Endocrinol. 47: 287, 1997).

The teachings of Culp et al., Douglas et al., Totsune et al., and Wilkinson et al. are as set forth above and differ from the invention as instantly claimed in not teaching natriuretic peptides as additional markers of heart failure.

Hall et al. teach the value of natriuretic peptide determinations, particularly N-terminal pro-brain natriuretic peptide and brain natriuretic peptide, in diagnosis and management of heart

failure patients. The reference teaches that the determinations should be combined with other diagnostic examinations, including other peptide determinations, and not as a stand alone test, to improve diagnostic performance. The reference does not, however, teach reagents for the determinations.

Either of Hunt et al. or Karl et al. teach immunoassay reagents and methods for determinations of natriuretic peptides for diagnosis of cardiac impairment.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have combined determinations of natriuretic peptides for diagnosis of heart failure, as taught in Hall, Hunt et al., and Karl et al., with determinations of other diagnostic markers, such as the determinations of urotensin II taught in Culp et al., as modified above, in view of the suggestion in Hall to combine tests to improve diagnostic performance.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Armbruster et al. (EP 1 241 479 A2) teach immunoassays of urotensin II for diagnosis of cardiovascular diseases.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JLG

James L. Grun, Ph.D.
June 16, 2006

Christopher L. Chin

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GROUP ~~1800~~ 1641